REMARKS

This response after final rejection is submitted because Applicants believe that all claims now presented are in condition for allowance. In any case entry of this response will place the application in better form for appeal. Applicants have added no new matter and have raised no new issues. Finally the arguments presented herein are in direct response to points raised by the Examiner in the last office action, and Applicants could not have filed their response at an earlier date.

Applicants note that this Response After Final Rejection is accompanied by a Petition for Revival Under 37 CFR 1.137(b), that is a petition for revival on the grounds that the abandonment of this application was unintentional.

The Examiner has prepared a confusing official action because on page 3 she has finally rejected claims 1,2,5,8,9,12,13,14,17,18,20,22,24,26 and 28 as obvious under 35 USC 103 in view of the same combination of prior art references as applied previously. Yet the Examiner notes that Applicants have canceled all of these claims and replaced those claims with claims 71 through 100. The Examiner then extends the rejection of the original claims to the elected species claim 80 through 86.

Applicants believe that focusing on pages 7 and 8 provides the best way to analyze the office action and to provide a point-by-point response to each of the Examiner's arguments. At the outset the Examiner and Applicants have a significant difference in opinion over what EP 0 509 761 to SZABO et al discloses and over what the POUYANI et al discloses and how close the disclosure in these reference comes to the presently claimed invention. The Examiner now admits on page 7, second full paragraph of the office action, that SZABO et al does not disclose lyotropic liquid crystal compositions that contain either hyaluronic acid, sodium hyaluronate or zinc hyaluronate. In the first paragraph of page 10 of the preceding office action, the Examiner argued that the SZABO lyotropic liquid crystal compositions did contain hyaluronic acid. Since SZABO et al serves as the Examiner's chief reference in the combination of references applied against the claims, Applicants wish to go over every difference between the SZABO lyotropic liquid crystal compositions and those in the present elected species claims 80 through 86.

The Applicants use sodium hyaluronate or zinc hyaluronate as the liquid crystal forming polymer. SZABO et al use PEG 35 000. The Examiner has not provided any evidence that sodium hyaluronate or zinc hyaluronate is an art-recognized equivalent of PEG 35 000 and the fact that Applicants use the sodium or zinc hyaluronate in an aqueous system and SZABO et al uses the PEG 35 000 in an

anhydrous system provides further evidence that the hyaluronates and the PEG 35 000 are not equivalent.

The Applicants in their elected species of claim 80 use an estrogen/progestin combination of hormone replacement drugs as the active ingredients whereas SZABO et al uses deprenyl, an MAO inhibitor as the active ingredient.

The Applicants' liquid crystal gel contains both a non-aqueous component and an aqueous component. The SZABO et al liquid crystal gel is anhydrous.

The Applicants liquid crystal gel specifically includes polyoxyethylene-glyceryl-trioleate as surfactant, which is not disclosed in the SZABO et al compositions.

The Applicants' compositions also include isopropyl myristate as a surfactant and this compound is not found in the SZABO et al compositions.

Applicants believe that the cited combination of the prior art references SZABO et al, BUNSCOHTEN et al, PARAB PV, BRYNHILDSEN et al, in further view of POUYANI et al provides no basis to reject any claim now presented as obvious under 35 USC 103 for the following reasons:

1. In the first full paragraph on page 7, the Examiner argues that SZABO et al discloses transdermal compositions containing both oil and water as well as anhydrous transdermal compositions. The Examiner points to page 2, lines 25 to 30 of SZABO et al. Applicants believe that the Examiner's citation of this passage is entirely misleading because this passage relates to the prior art cited in SZABO et al, which is a completely different composition from the anhydrous transdermal compositions disclosed in SZABO et al further down the page starting on line 32. The transdermal basic ointments disclosed in SZABO et al on page 2, line 25 are not lyotropic liquid crystal compositions and have nothing to do with lyotropic liquid crystal compositions. Thus Applicants maintain that the only lyotropic liquid crystalline compositions disclosed in SZABO et al are anhydrous.

2. In the presently claimed lyotropic liquid crystal compositions, Applicants use sodium hyaluronate or zinc hyaluronate, whereas in SZABO et al the inventors specifically use Polyoxyethylene 35 000 or any similar polymer having a coilness characterizing a value of >0.6. Applicants emphasize that structurally this polymer is far removed from either sodium hyaluronate or zinc hyaluronate. Furthermore, Applicants see no reason that one "skilled in the art" would substitute sodium

hyaluronate or zinc hyaluronate for the PEG 35 000 disclosed in SZABO et al.

3. The Examiner admits in the first full paragraph of page 4 of the office action that SZABO et al does not disclose either zinc or sodium hyaluronate or hormones such as estrogen in the lyotropic liquid crystalline compositions therein. However, at the bottom of page 7 the Examiner re-asserts that she can correctly combine SZABO et al with BUNSCHOTEN et al because SZABO et al discloses lyotropic liquid crystalline compositions for transdermal administration of a pharmaceutically active agent, and BUNSCHOTEN et al discloses transdermal administration of estrogen and progestin hormones with hydrophilic polymers, such as polycarbophil and polyvinylpyrrolidine in a gel composition. However, there are two missing elements from the Examiner's argument: the disclosure of the gel compositions in BUNSCHOTEN et al makes no mention of lyotropic liquid crystalline compositions and makes no mention of either sodium hyaluronate or zinc hyaluronate, which are structurally far removed from either polycarbophil and polyvinylpyrrolidine. Thus Applicants maintain that the combination of SZABO et al and BUNSCHOTEN et al falls far short of suggesting the presently claimed invention.

4. The Examiner admits that none of the SZABO et al, BUNSCHOTEN et al, and PARAB references discloses sodium hyaluronate

or zinc hyaluronate in the preparation of lyotropic liquid crystalline compositions for transdermal administration of estrogen/progestin hormones or of any other pharmaceutically active ingredients. However at the bottom of page 7 of the office action, the Examiner argues that POUYANI et al discloses that the salt form of hyaluronic acid (HA) increases the ability of HA to be a good drug carrier. Applicants do not agree with the Examiner's interpretation of POUYANI et al. In the paragraph at the bottom of col. 3 going onto column 4, the reference discusses the instability of hyaluronic acid. In the first paragraph in col. 4 of the reference it is stated that hyaluronic acid naturally occurs in the form of its sodium salt. Nowhere does the reference say, however, that the sodium salt of hyaluronic acid is a better form of hyaluronic acid to serve as a drug carrier than hyaluronic acid per se. In fact the whole point of POUYANI et al is to provide a more stable form of hyaluronic acid by functionalizing the hyaluronic acid or sodium hyaluronate with dihydrazide. See col. 4 of the reference.

4a. Thus the Examiner misreads POUYANI et al when she states that the reference discloses that sodium hyaluronate is a better form of hyaluronic acid than HA per se to serve as a drug carrier and concludes that the reference discloses that hyaluronic acid or sodium hyaluronate per se (non-functionalized) would be stable enough to serve as a drug carrier. Col. 4, lines 7 and 8

indicates only that hyaluronate often occurs naturally as the sodium salt, sodium hyaluronate, but does not say that sodium hyaluronate is more stable than hyaluronic acid. When the Examiner points out that POUYANI et al in col. 3, lines 60 to 65 states that hyaluronate possesses a number of characteristics that make it advantageously used as a drug carrier, that it is biocompatible, non-immunogenic, subject to natural degradation by enzymes, and possesses OH, COOH, and CH_2OH groups that may be covalently modified, she reads only what she wants to read, and disregards the rest that follows after line 65 of col. 3, where POUYANI et al discusses the instability of hyaluronate and the need to modify it by functionalizing it with dihydrazide in order to increase stability. According to col. 3, line 65 to col. 4, line 2:

"However, hyaluronate is known to be unstable and undergoes degradation below a pH of about 2 and above about pH 9. The mild reaction conditions used in the invention avoid this degradation. Moreover, the modified products show improved resistance to pH extremes."

Thus POUYANI et al requires the functionalization to stabilize the hyaluronate so that the hyaluronate may serve as an adequately stable drug carrier and therefore discourages the use of salts of hyaluronic acid per se, without the functionalization, as drug carriers.

5. PARAB discloses only that a mixture of dibutyl adipate and isopropyl myristate is a good transdermal penetrant. There is no disclosure, however, of isopropyl myristate per se as a transdermal penetrant. Furthermore the fact that the combination of SZABO et al, BUNSCHOTEN et al and POUYANI et al is faulty is, by no means, cured by the citation of PARAB.

6. The BRYNHILDSEN et al reference relates to a transdermal patch and not to a lyotropic liquid crystal gel according to the present invention. Applicants disagree with the Examiner's statement at the top of page 8 of the office action that the present claims while directed to a transdermal liquid crystalline gel, do not avoid a transdermal patch. In the prior art there is a sharp distinction between a transdermal patch and a transdermal gel as transdermal delivery systems for a pharmaceutical. See paragraph [0091] of BUNSCHOTEN et al which draws a clear distinction between patches and gels as transdermal delivery system for pharmaceuticals.

In view of the above Applicants believe that the Examiner has failed to provide a basis for the rejection of any of the examined claims 80 through 86 as obvious in view of the cited prior art. Therefore the Applicants ask that the Examiner lift this basis for the rejection of these claims under 365 USC 103 as obvious.

Applicants note that the Examiner has withdrawn from further consideration claims 71 through 79 and 87 through 100 as directed to a non-elected invention. In Applicants' opinion the Examiner has not found prior art sufficient to reject claims 80 through 86, the elected group, and so she should expand her search of the prior art and examine claims 71 through 79 and 87 through 100 as well.

Applicants believe that claims 80 through 86 are in condition for allowance and Applicants earnestly solicit a response to that effect.

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Enclosure:
Petition for Revival Under 37 CFR 1.137(b)